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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/234,028	01/20/1999	RONALD T. RAINES	960296.95360	6579

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EXAMINER	
HUTSON, RICHARD G	
ART UNIT	PAPER NUMBER
1652	

NOTIFICATION DATE	DELIVERY MODE
12/12/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

pat-dept@quarles.com

Office Action Summary	Application No.	Applicant(s)	
	09/234,028	RAINES, RONALD T.	
	Examiner	Art Unit	
	Richard G. Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *7/31/2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,5,7,9 and 18-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4, 5, 7, 9 and 18-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants amendment of claims 1, 4, 5, 7, 9, and the addition of new claims 21-23, in the paper of 7/31/2008, is acknowledged. Claims 1, 4, 5, 7, 9 and 18-23 are at issue and are present for examination.

Applicants' arguments filed on 7/31/2008, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Objections

Claims 19, 21-23 are objected to because of the following informalities:

Claim 19 is objected to because claim 19 is directed to an RI variant of claim 18, the residues at positions 329 and 330 being alanine residues. Claim 19 appears to be improperly dependent on claim 18, in that it does not further limit that RI variant of claim 18, that has a difference that consists of an alanine residue at position 95, 96, 329 ***or*** 330. The discrepancy between the claimed differences which consist of mutations at positions described with “or” versus “and” is the basis of this objection. Claims 21-23 are similarly objected to for the same reason as discussed above for claim 19, relative to the claims from which they are dependent on.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4, 5, 7, 9 and 18-23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection was stated in the previous office action as it applied to previous claims 1, 4, 5, 7, 9 and 18-20. In response to the previous rejection, applicants have amended claims 1, 4, 5, 7, 9, and added new claims 21-23, and traverse the rejection as it applies to the newly amended claims. Newly added claims 21-23 are included in this rejection for the reasons previously stated for claims 1 , 4, 5, 7, 9 and 18-20.

Applicants continue to traverse the rejection as previously, on the basis that applicants previous amendment was made with the intention that the presented claims embraced "the situation wherein the only variation from the reference sequence is that 'at least one of the residues at [the recited positions is]an alanine.'" Applicants submit that applicant's most recent amendment accommodates applicant's intent, while addressing the Examiner's previous concerns. Applicants submit that "the difference consists of an alanine residue" at a recited position. Applicants note that they do not intend the amended claim language to require an alanine at only one recited residue

position in each claimed ribonuclease inhibitor (RI) variant, but rather still to literally encompass variants where any of the recited residue positions is an alanine.

Applicants amendment of the claims and applicants argument are acknowledged, however, these continue to be insufficient to overcome the current rejection because applicant's amendment continues to describe the the/a difference between the claimed RI variant and a reference RI variant (SEQ ID NO: 3 or SEQ ID NO:2) without describing the rest of the RI variant structure.

While applicant's amendment and discussion addresses the differences of a claimed RI variant, it remains that applicant's amendment still has not limited the scope of the claimed product and the scope of the claimed product continues to not be adequately described for the reasons previously stated.

Applicants continue to be reminded that while applicants specification provides examples of ribonuclease inhibitor variants that are encompassed by the claims, two species is not sufficient to adequately describe the genus of claims which still appear to be ill defined with regard to that structure of the RI variant outside of the discussed differences. The specification fails to describe sufficient representative species of these ribonuclease inhibitor variants by sufficient structural characteristics or properties other than the activities recited in claim 1 and the disclosed cysteine modifications differences, for which no predictability of overall structure is apparent. Given this lack of additional representative species or overall RI variant structure as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full,

clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1, 4, 5, 7, 9 and 18-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a mutant ribonuclease inhibitor comprising the amino acid sequence of SEQ ID NO: 3, wherein said mutation is a substitution in one of its two adjacent cysteine residues to an amino acid residue not capable of forming a disulfide bond, the mutant ribonuclease inhibitor having a greater resistance to oxidation, the mutant ribonuclease inhibitor retaining its specificity and binding affinity to ribonuclease, does not reasonably provide enablement for any variant ribonuclease inhibitor differing from references SEQ ID NO: 3 or 2 wherein the difference consists of an alanine residue at position 95, 96, 329 and 330, relative to SEQ ID NO: 3 and wherein the difference consists of an alanine residue at positions 324 and 325, relative to SEQ ID NO: 2, the mutant ribonuclease inhibitor having a greater resistance to oxidation and retaining its specificity and binding affinity to ribonuclease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection was stated in the previous office action as it applied to previous claims 1, 4, 5, 7, 9 and 18-20. In response to the previous rejection, applicants have amended claims 1, 4, 5, 7, 9, and added new claims 21-23, and traverse the rejection as it applies to the newly amended claims. Newly added claims 21-23 are included in this rejection for the reasons previously stated for claims 1 , 4, 5, 7, 9 and 18-20.

Applicants traverse this rejection in combination with the rejection above on the basis that applicants previous amendment was made with the intention that the presented claims embraced "the situation wherein the only variation from the reference sequence is that 'at least one of the residues at [the recited positions is]an alanine.'" Applicants submit that applicant's most recent amendment accommodates applicant's intent, while addressing the Examiner's previous concerns. Applicants submit that "the difference consists of an alanine residue" at a recited position. Applicants note that they do not intend the amended claim language to require an alanine at only one recited residue position in each claimed ribonuclease inhibitor (RI) variant, but rather still to literally encompass variants where any of the recited residue positions is an alanine.

As discussed above, applicants amendment of the claims and applicants argument are acknowledged, however, these continue to be insufficient to overcome the current rejection because applicant's amendment continues to describe the/a difference between the claimed RI variant and a reference RI variant (SEQ ID NO: 3 or SEQ ID NO:2) without describing the rest of the RI variant structure.

With respect to the enablement of the claimed genus, applicants specification does not support the broad scope of the claims which encompass all modifications and

fragments of any mutant ribonuclease inhibitor which does not comprise said cysteine mutations because the specification does not establish: (A) regions of the protein structure which may be modified without effecting ribonuclease inhibitor activity and oxidative resistance; (B) the general tolerance of ribonuclease to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of amino acid modifications of any ribonuclease inhibitor. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those mutants having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is 571-272-0930. The examiner can normally be reached on M-F, 7:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat T. Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

rgh
12/7/2008

/Richard G Hutson/
Primary Examiner, Art Unit 1652